

**CLAIMS**

1. A method of modulating NF- $\kappa$ B induction in a cell comprising contacting a cell with an effective amount of an anti-inflammatory compound comprising at least one NEMO binding domain, thereby modulating NF- $\kappa$ B induction in a cell.
2. The method of claim 1, wherein the anti-inflammatory compound is capable of blocking the interaction between one or more IKKs and NEMO.
3. The method of claim 2, wherein the IKK is selected from the group consisting of IKK $\alpha$  and IKK $\beta$ .
4. The method of claim 1, wherein the anti-inflammatory compound further comprises at least one membrane translocation domain.
5. The method of claim 1, wherein the NEMO binding domain comprises the amino acid sequence set forth in SEQ ID NO:2, 4, 5, 6, 11, 12, 16 or 17.
6. A method for treating a subject suffering from an inflammatory disorder comprising administering to said subject an anti-inflammatory compound in an amount effective to treat said subject suffering from an inflammatory disorder.
7. The method of claim 6, wherein the anti-inflammatory compound is capable of inhibiting the recruitment of leukocytes into sites of acute and chronic inflammation.
8. The method of claim 6, wherein the anti-inflammatory compound is capable of down-regulating the expression of E-selectin on endothelial cells.
9. The method of claim 6, wherein the anti-inflammatory compound is capable of inhibiting osteoclast differentiation.

10. A method of modulating NF- $\kappa$ B-dependent target gene expression in a cell comprising contacting a cell with an effective amount of an anti-inflammatory compound comprising at least one NEMO binding domain, thereby modulating NF- $\kappa$ B-dependent target gene expression in a cell.

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11. The method of claim 10, wherein the anti-inflammatory compound is capable of blocking the interaction between one or more IKKs and NEMO.

12. The method of claim 11, wherein the IKK is IKK $\beta$ .

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13. The method of claim 10, wherein the NF- $\kappa$ B-dependent target gene is E-selectin.

14. A method of identifying a compound capable of interacting with NEMO, comprising exposing cells which express NEMO and NF- $\kappa$ B to a test compound and (determining whether the test compound modulates activation of NF- $\kappa$ B by the cell, wherein an alteration in activation of NF- $\kappa$ B is indicative of a compound which is capable of interacting with NEMO.

15. A method of identifying a compound which modulates an activity of NEMO, comprising exposing cells which express NEMO to a test compound and determining whether the test compound modulates an activity of NEMO, thereby identifying a compound which modulates an activity of NEMO.

16. An anti-inflammatory compound comprising a NEMO binding domain fused with at least one membrane translocation domain.

17. The anti-inflammatory compound of claim 16, wherein the membrane translocation domain facilitates membrane translocation *in vivo*.

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18. The anti-inflammatory compound of claim 16, wherein the membrane translocation domain is selected from the group consisting of the third helix of the *antennapedia* homeodomain and HIV-1 Tat protein.

19. The anti-inflammatory compound of claim 16, wherein the NEMO binding domain comprises the amino acid sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17.

20. A composition comprising the anti-inflammatory compound of any one of claims 16, 17, 18, or 19.

21. The composition of claim 20, further comprising a pharmaceutically acceptable carrier.

22. An isolated peptide selected from the group consisting of:

(a) an isolated peptide comprising the amino acid sequence set forth in SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17, 18 or 19;

10 (b) an isolated peptide comprising a fragment of at least three amino acids of the amino acid sequence set forth in SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19;

15 (c) an isolated peptide comprising a conservative amino acid substitution in the amino acid sequence set forth in SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19; and

(d) a naturally occurring amino acid sequence variant of the amino acid sequence set forth in SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19.

23. An isolated peptide consisting of the amino acid sequence of SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

24. A composition comprising the peptide of any one of claims 22 or 23.

25. The composition of claim 24, further comprising a pharmaceutically acceptable carrier.

26. An isolated nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19; and

30 (b) an isolated nucleic acid molecule that encodes a fragment of at least three amino acids of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

27. A method of treating an NFkB-mediated condition in a subject, comprising administering to the subject an effective amount of an anti-inflammatory compound which inhibits binding of NEMO to an IKK.

28. The method of claim 27, wherein the NFkB-mediated condition is an inflammation disorder, an autoimmune disease, transplant rejection, osteoporosis, cancer, Alzheimer's disease, atherosclerosis, a viral infection, or ataxia telangiectasia.

5 29. The method of claim 28, wherein the inflammation disorder is selected from the group consisting of asthma, allergies, urticaria, anaphylaxis, cutaneous inflammation, sepsis, psoriasis, rheumatoid arthritis, osteoarthritis, psoriatic arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease, vasculitis, and bursitis.

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30. The method of claim 28, wherein the inflammation disorder is selected from the group consisting of dermatitis, eczema, psoriasis, osteoarthritis, psoriatic arthritis, lupus and spondylarthritis.

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31. The method of claim 27, wherein the anti-inflammatory compound is capable of blocking the interaction between an IKK and NEMO.

32. The method of claim 27, wherein the anti-inflammatory compound comprises a NEMO binding domain and at least one membrane translocation domain.

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33. The method of claim 32, wherein the membrane translocation domain is selected from the group consisting of the third helix of the *antennapedia* homeodomain and HIV-1 Tat protein.

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34. The method of claim 32, wherein the NEMO binding domain comprises the amino acid sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17.

30 35. An anti-inflammatory compound comprising the amino acid sequence DRQIKIWFQNRRMKWKKTALDWSWLQTE.